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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,803	05/22/2001	Jeffrey J. Rade	71699/55591	8907

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,803	RADE ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,30,33-49 and 52-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29, 30, 33-49, 52-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 8/8/05 have been entered. Claims 29, 30, 33, 34, 45, 48, 52, 56, 59 have been amended. Claims 31, 32, 50, 51 have been canceled. Claims 68-72 are newly submitted. Claims 29, 30, 33-49, 52-72 are pending and under current examination.

A telephone interview was conducted on 10/17/05 with applicant's representative Mr. Robert Buchanan discussing the standing rejections in view of the amendment. The content of the discussion is reflect below.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and persuasive argument will not be reiterated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification as originally filed does not describe the invention as now claimed.

The newly submitted claims 70-72 recite "early graft failure" or "an artificial graft", which graft encompasses any organ and tissue graft, not limited to "vascular or vein graft" as originally disclosed. As such, the amendment broadens the scope of the

invention. Further, applicants failed to specifically point out where in the specification the support for the broadly claimed artificial graft could be found. Applicants are reminded that the original disclosure is entitled "Genetic engineering of vascular grafts to resist disease", and throughout the specification, vascular graft is consistently the subject of the graft. The original disclosure is silent concerning other types of graft failure. Accordingly, the amendment improperly broadened the scope of the invention and introduced new matter into the specification.

MPEP 2163.02 teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION". Since the amendment has added or improperly broadened the scope of the original disclosure, the amendment is a departure from or an addition to the disclosure of the application as filed, thus it introduces new matter into the disclosure.

For reasons set forth above, the amendments filed 8/8/05 are objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action. Alternatively, Applicant are invited to specifically point out where in the specification the support can be found for the amendment made to the disclosure.

To the extent that the claimed methods are not adequately described in the instant disclosure, claims 70-72 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described, which is not conventional in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29, 30, 33-49, 52, 59, 60, 61 stand rejected and claims 68-72 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Vassalli et al* (Cardiovasc Res 1997;35:459-69), in view of *Waugh et al* (Circ Res 1999;84:84-92, IDS) and *Thomas et al* (Transplant 1999;68:1660-73).

The amended and new claims are directed to a method for treating a mammal to resist early vein graft failure by introducing into autologous endothelial cells of a vein graft an effective amount of a nucleic acid encoding a thrombomodulin (TM), wherein the nucleic acid further encodes a NF-kB inhibitor (IκB). The specification teaches that

early graft failure is typically due to occlusive *thrombosis* (Specification, page 1, last paragraph and claim 37).

Applicants argued that that Waugh used arterial angioplasty which stretches and damages the artery and destroys the intimal endothelial cells, and Waugh teach prevent clots from the site of balloon injury of an artery, wherein the endothelial cells were stripped away by the balloon.

In response, Applicant's attention is directed to the section bridging pages 85 and 86 of *Waugh et al*, where they teach to isolating a 3.0-cm segment of the inferior epigastric artery beginning just proximal to the left IEA stump from circulation, and via "atraumatic microvascular clamps", gently washed the lumen, and incubating the segment with Adv-THM. Three days later, thrombus was initiated by dividing and reanastamosing the segment of CFA (column 1, page 86). Here, there is not balloon angioplasty performed. Since it takes another round of surgery to initiate the thrombus, it implies the endothelium was largely intact at the time of the local delivery of the recombinant viral vector.

Moreover, *Waugh* reference was relied on for the feasibility and effect of *in vivo* expressing THM. Assuming that the stasis/injury model taught by *Waugh et al* did strip away endothelial cells, the fact that it reduced or prevented thrombosis indicating that the delivered Ad-THM has somewhat substituted/replaced the function of the vascular endothelium. *Waugh et al* has made clear that the TM is normally secreted by the endothelial cells and plays a central role in hemostasis (e.g. abstract).

Applicant then argued that Waugh et al performed experiment in artery, not vein, and the differences between vein and artery grafts are substantial and non-obvious.

In response, although artery has more smooth muscle cells in the media layer, both artery and vein grafts contain endothelial cells, which is the functional site of the THM. The specification as filed teach vascular graft as a whole encompassing both vein and artery grafts, and using vein graft in peripheral arterial bypass surgeries (e.g. Specification, page 1, lines 20-26). This teaching is consistent with the skilled in the art at the time. For example, *Vassalli et al* teach, "Small-diameter prosthetic vascular grafts are inferior to autologous arteries and veins in both coronary arterial and infrainguinal revascularization procedures" (§ 2.7, emphasis added). It appears neither the skilled artisan nor the specification as filed consider there is substantial and non-obvious differences between vein and artery grafts.

New claims 70-72 are drawn to a method of making an artificial graft and graft made. As cited *supra*, such is obviously taught by *Vassali et al* (prosthetic vascular graft), here the product is neutral to vein or artery because it is an artificial support lying under the endothelial layer.

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claims 53-55, and 62-64 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Vassalli et al* (Cardiovasc Res 1997;35:459-69), in view of *Waugh et al* (Circ Res 1999;84:84-92, IDS) and *Thomas et al* (Transplant 1999;68:1660-73) as

applied to claims 29, 30, 33-49, 52, 59, 60-72 above, and further in view of *Hardy et al* (J Virol 1997;71:1842-9), for reasons of record and *supra*.

Claims 56-58, and 65-67 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Vassalli et al* (Cardiovasc Res 1997;35:459-69), in view of *Waugh et al* (Circ Res 1999;84:84-92, IDS) and *Thomas et al* (Transplant 1999;68:1660-73) as applied to claims 29-50, 52, 59, 60, 61 above, and further in view of *Qing et al* (J Virol 1997;71:5663-7), for reasons of record and *supra*.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
October 20, 2005